

| | | | | | |
|--------------|------------|------------------|-------|------------------|------------|
| Flag-peptide | GAD65 | Not I | IA2 | Not I | poly-his |
| DYKDDDDK | ----- | Sgf I | ----- | Sgf I | ----- |
| | KKKRRPRKKK | | | KKKRRPRKKK | CNGSHHHHHH |

FIG. 1a

| | | | | | |
|--------------|------------|------------------|-------|------------------|------------|
| Flag-peptide | GAD65 | Sgf I | IA2 | Sgf I | poly-his |
| DYKDDDDK | ----- | Not I | ----- | Not I | ----- |
| | KKKRRSRKKK | | | KKKRRSRKKK | CNGSHHHHHH |

FIG. 1b

~~1A2 Underlined aa 771-979 Accession No. L18983~~

MRRPRRPGGLGGGGLRLLCLLLSSRPGGCSA VSAHGCLFDRRLCSHLEVCIQDGLFGQCQVGVQARPLLQVTSPVLQRL
QGVLRQLMSQGLSWHDDLQYVISQEMERIPRLRPPPRDRSGLAPKRPGPAGELLQDIPGSA PAAQHRLPQPPVKGKG
AGASSLSPLQAELLPLLEHLLPPQPPHPSLSYEPALLQPYLFHQFGSRDGSRVSESGPMVSVGPLPKAEAPALFSRTASKGI
FGDHPGHSYGDLPGPSPAQLFQDSGLLYLAQELPAPSRARVPRLPEQGSSSRAEDSPEGYEKEGLDGRGEKPASPAVQPDAAAL
QRLAAVLAGYGVELRQLTPEQLSTLLTLQLLPKGAGRNPGGVNVGADIKKTMEGPVEGRDTAELPARTSPMPGHPTASPT
SSEVQQVPSVPSSEPPKAAARPPVTPVLLLEKKSPLGQSQPTVAGQPSARPA AEEYGYIVTDQKPLSLAAGVKLLEILAEHVHMSS
GSFINISVVGPALETRIRHNEQNLSLADVTTQAGLVKSELEAQTGLQILQTGVGQREEAA VLPQTAHSTSPMRSVLLTLVALA
GVAGLLVALAVALCVRHARQQDKERLAALGPEGAHGDTTFEYQDLCRQHMAATKSLFNRAEGPPEPSRVSSVSSQFSDAAQ
ASPSHSSTPWCPEPAQANMDISTGHMILAYMEDHLNRDRLAKEWQALCA YQAEPTCA TAQEGEKNKKNRHPDFLPYDH
ARIKLVESSPSRSDYINASPIEHDPMPAYIATQGPLSHTIADFWMVWESGCTVIVMLTPLVEDGVKQCDR YWPDEGASLY
HVYEVNLVSEHWCEDFLVRSFYLNKVNQTOETRTLTOFHFLSWPAEGTPASTRPLLDERRKVNKCYGRGRSCPIIVHCSDGAGR
TGTYILIDMVLNRMAKGVKEIDIAATLEHVRDORPGLVRSKDOFEFALTAVAAEEVNAILKALPQ

FIG. 2a

~~GAD65 Underlined aa102-585 Accession No. M74826~~

MASPGSGFWSFGSEDGSDENPGTARAWCQVAQKFTGGIGNKL CALLYGD AEKPAESGSGQPPRAAARKAAACADQKPCS
CSKV DVNYAFLHATDLLPACDGERPTLAFLQDV MNILLO YVVKSFDRSTKVIDFHYPNELLOEYNWELADQPNLEILMHC
QTTLKYAIKTGHPRYFNQLSTGLDMVGLAADWLTTSTANTNMFTYEIAPVFLLEYVTLK KMREIIGWPGSGDGI FSPGGAIS
NMYAMMIARFKMFPEVKEKGMAALPRLJAFITSEHSFSLKKGAAALGIGTDSVILKCDERGMIPSDLERRILEAKQKGFVPF
LVSATAGTTVYGAFDPLLA VADICKKYKIWMHVDAAWGGGLMSRKHKKWKL SGVERANSVTWNP HKMMGVPLQCSALLY
REEGLMONCNOMHASYLEQODKHYDLSYDTGDKALOCGRHVDVFKLWLMWRAKGITTGFEAHVDKCLEAEYL YNIIKNR
EGYEMVFDGKPKOHTNVCFWYIPPSLRTLEDNEERM SRLSKVAPVIKARMMEYGTIMVSYOPLGDKVNFERRMVISNPAATHQ
DIDFLIEEIERLGQDL

FIG. 2b

~~Translation Human preproinsulin.~~

~~EMBL accession nr. v00565~~

MALWMRLPLALLALWGPDPA AAFVNQHL CGSHLVEALYLVCGERGFFYT
PKTRREAEDLQVGQVELGGPGAGSLQPLALEGSLQKRGIVEQCCTSI CSLYQ
LENYCN

FIG. 2c

Human GAD65 nucleotide sequence

M74826 Length: 2457 September 1, 1995 12:22 Type: N Check: 8038 ..

1 ACCCGCCCTC GCCGCTCGGC CCCGCGCGTC CCCGCGCGTG CCCTCCTCCC
51 GCCACACGGC ACGCACGCGC GCGCAGGGCC AAGCCGAGGC AGCCGCCCCG
101 AGCTCGCACT CGCTGGCGAC CTGCTCCAGT CTCAAAGCC GATGGCATCT
151 CCGGGCTCTG GCTTTTGGTC TTTCGGGTCG GAAGATGGCT CTGGGGATTC
201 CGAGAATCCC GGCACAGCGC GAGCCTGGTG CCAAGTGGCT CAGAAGTTCA
251 CGGGCGGCAT CGGAAACAAA CTGTGCGCCC TGCTCTACGG AGACGCCGAG
301 AAGCCGGCGG AGAGCGGCGG GAGCCAACCC CCGCGGGCCG CCGCCCGGAA
351 GGCCGCCTGC GCCTGCGACC AGAAGCCCTG CAGCTGCTCC AAAGTGGATG
401 TCAACTACGC GTTTCTCCAT GCAACAGACC TGCTGCCGGC GTGTGATGGA
451 GAAAGGCCCA CTTTGGCGTT TCTGCAAGAT GTTATGAACA TTTTACTTCA
501 GTATGTGGTG AAAAGTTTCG ATAGATCAAC CAAAGTGATT GATTTCATT
551 ATCCTAATGA GCTTCTCCAA GAATATAATT GGGAATTGGC AGACCAACCA
601 CAAAATTTGG AGGAAATTTT GATGCATTGC CAAACAAC TC TAAATATGC
651 AATTAAAACA GGGCATCCTA GATACTTCAA TCAACTTTCT ACTGGTTTGG
701 ATATGGTTGG ATTAGCAGCA GACTGGCTGA CATCAACAGC AAATACTAAC
751 ATGTTACCT ATGAAATTGC TCCAGTATTT GTGCTTTTGG AATATGTCAC
801 ACTAAAGAAA ATGAGAGAAA TCATTGGCTG GCCAGGGGGC TCTGGCGATG
851 GGATATTTTC TCCCGGTGGC GCCATATCTA ACATGTATGC CATGATGATC
901 GCACGCTTTA AGATGTTCCC AGAAGTCAAG GAGAAAGGAA TGGCTGCTCT
951 TCCCAGGCTC ATTGCCTTCA CGTCTGAACA TAGTCATTTT TCTCTCAAGA
1001 AGGGAGCTGC AGCCTTAGGG ATTGGAACAG ACAGCGTGAT TCTGATTAAA
1051 TGTGATGAGA GAGGGAAAAT GATTCCATCT GATCTTGAAA GAAGGATTCT
1101 TGAAGCCAAA CAGAAAGGGT TTGTTCTTTT CCTCGTGAGT GCCACAGCTG
1151 GAACCACCGT GTACGGAGCA TTTGACCCCC TCTTAGCTGT CGCTGACATT
1201 TGCAAAAAGT ATAAGATCTG GATGCATGTG GATGCAGCTT GGGGTGGGGG
1251 ATTACTGATG TCCCGAAAAC ACAAGTGGAA ACTGAGTGGC GTGGAGAGGG

FIG. 3a

~~Human IA-2 nucleotide sequence~~

~~L18983 Length: 3613 November 20, 1997 16:45 Type: N Check: 6409~~

1 CAGCCCCTCT GGCAGGCTCC CGCCAGCGTC GCTGCGGCTC CGGCCCCGGA
51 GCGAGCGCCC GGAGCTCGGA AAGATGCGGC GCCCGCGGCG GCCTGGGGGT
101 CTCGGGGGAT CCGGGGGTCT CCGGCTGCTC CTCTGCCTCC TGCTGCTGAG
151 CAGCCGCCCC GGGGGCTGCA GCGCCGTTAG TGCCACGGC TGTCTATTTG
201 ACCGCAGGCT CTGCTCTCAC CTGGAAGTCT GTATTCAGGA TGGCTTGTTT
251 GGGCAGTGCC AGGTGGGAGT GGGGCAGGCC CGGCCCCTTT TGCAAGTCAC
301 CTCCCCAGTT CTCCAACGCT TACAAGGTGT GCTCCGACAA CTCATGTCCC
351 AAGGATTGTC CTGGCACGAT GACCTCACCC AGTATGTGAT CTCTCAGGAG
401 ATGGAGCGCA TCCCCAGGCT TCGCCCCCA GAGCCCCGTC CAAGGGACAG
451 GTCTGGCTTG GCACCCAAGA GACCTGGTCC TGCTGGAGAG CTGCTTTTAC
501 AGGACATCCC CACTGGCTCC GCCCTGCTG CCCAGCATCG GCTTCCACAA
551 CCACCAGTGG GCAAAGGTGG AGCTGGGGCC AGCTCCTCTC TGTCCCCTCT
601 GCAGGCTGAG CTGCTCCCGC CTCTCTTGA GCACCTGCTG CTGCCCCAC
651 AGCCTCCCCA CCCTTCACTG AGTTACGAAC CTGCCTTGCT GCAGCCCTAC
701 CTGTTCCACC AGTTTGGCTC CCGTGATGGC TCCAGGGTCT CAGAGGGCTC
751 CCCAGGGATG GTCAGTGTCG GCCCCCTGCC CAAGGCTGAA GCCCCTGCCC
801 TCTTCAGCAG AACTGCCTCC AAGGGCATAT TTGGGGACCA CCCTGGCCAC
851 TCCTACGGGG ACCTTCCAGG GCCTTCACCT GCCCAGCTTT TTCAAGACTC
901 TGGGCTGCTC TATCTGGCCC AGGAGTTGCC AGCACCAGC AGGGCCAGGG
951 TGCCAAGGCT GCCAGAGCAA GGGAGCAGCA GCCGGGCAGA GGAATCCCCA
1001 GAGGGCTATG AGAAGGAAGG ACTAGGGGAT CGTGGAGAGA AGCCTGCTTC
1051 CCCAGCTGTG CAGCCAGATG CGGCTCTGCA GAGGCTGGCC GCTGTGCTGG
1101 CGGGCTATGG GGTAGAGCTG CGTCAGCTGA CCCCTGAGCA GCTCTCCACA
1151 CTCCTGACCC TGCTGCAGCT ACTGCCCAAG GGTGCAGGAA GAAATCCGGG
1201 AGGGGTTGTA AATGTTGGAG CTGATATCAA GAAAACAATG GAGGGGCCGG
1251 TGGAGGGCAG AGACACAGCA GAGCTTCCAG CCCGCACATC CCCCATGCCT

FIG. 3c

~~PREPROINSULIN.~~

~~Exon sequences, i.e. sequences to be used in the patent are underlined and represent exon sequences.~~

~~V00565 Length: 4992 December 18, 1997 17:50 Type: N Check: 9721 ..~~

1 CTCGAGGGGC CTAGACATTG CCCTCCAGAG AGAGCACCCA ACACCCTCCA
51 GGCTTGACCG GCCAGGGTGT CCCCTTCCTA CTTGGAGAG AGCAGCCCCA
101 GGGCATCCTG CAGGGGGTGC TGGGACACCA GCTGGCCTTC AAGGTCTCTG
151 CCTCCCTCCA GCCACCCAC TACACGCTGC TGGGATCCTG GATCTCAGCT
201 CCCTGGCCGA CAACACTGGC AAACCTCCTAC TCATCCACGA AGGCCCTCCT
251 GGGCATGGTG GTCCTTCCCA GCCTGGCAGT CTGTTCTCA CACACCTTGT
301 TAGTGCCAG CCCCTGAGGT TGCAGCTGGG GGTGTCTCTG AAGGGCTGTG
351 AGCCCCCAGG AAGCCCTGGG GAAGTGCCTG CTTGCCTCC CCCC GGCCCT
401 GCCAGCGCT GGCTCTGCCC TCCTACCTGG GCTCCCCCA TCCAGCCTCC
451 CTCCCTACAC ACTCCTCTCA AGGAGGCACC CATGTCCTCT CCAGCTGCCG
501 GGCCTCAGAG CACTGTGGCG TCCTGGGGCA GCCACCGCAT GTCCTGCTGT
551 GGCATGGCTC AGGGTGAAA GGGCGAAGG GAGGGTCTCT GCAGATAGCT
601 GGTGCCCCT ACCAAACCCG CTCGGGGCAG GAGAGCCAAA GGCTGGGTGT
651 GTGCAGAGCG GCCCCGAGAG GTCCGAGGC TGAGGCCAGG GTGGGACATA
701 GGGATGCGAG GGGCCGGGGC ACAGGATACT CCAACCTGCC TGCCCCATG
751 GTCTCATCCT CTTGCTTCTG GGACCTCCTG ATCCTGCCCC TGGTGCTAAG
801 AGGCAGGTAA GGGGCTGCAG GCAGCAGGGC TCGGAGCCCA TGCCCCCTCA
851 CCATGGGTCA GGCTGGACCT CCAGGTGCCT GTTCTGGGGA GCTGGGAGGG
901 CCGGAGGGGT GTACCCAGG GGCTCAGCCC AGATGACACT ATGGGGGTGA
951 TGGTGTCTATG GGACCTGGCC AGGAGAGGGG AGATGGGCTC CCAGAAGAGG
1001 AGTGGGGGCT GAGAGGGTGC CTGGGGGGCC AGGACGGAGC TGGGCCAGTG
1051 CACAGCTTCC CACACCTGCC CACCCCAGA GTCCTGCCGC CACCCCAGA
1101 TCACACGGAA GATGAGGTCC GAGTGGCCTG CTGAGGACTT GCTGCTTGTC
1151 CCCAGGTCCC CAGGTCATGC CCTCCTTCTG CCACCCTGGG GAGCTGAGGG
1201 CCTCAGCTGG GGCTGCTGTC CTAAGGCAGG GTGGGAATA GGCAGCCAGC
1251 AGGGAGGGGA CCCCTCCCTC ACTCCCACTC TCCACCCCC ACCACCTTGG
1301 CCCATCCATG GCGGCATCTT GGGCCATCCG GGAAGGGGA CAGGGGTCTT
1351 GGGGACAGGG GTCCGGGGAC AGGGTCTTGG GGACAGGGGT GTGGGGACAG

FIG. 3f